## **Association between plasma procalcitonin with onset of MACE, in patients with Acute ST elevated MI: An Unicentric Prospective Observational Comparative Study**

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## **Introduction:**

Cardiovascular diseases (CVDs) represent a leading cause of premature mortality globally. It contributes to 17.7 million deaths annually which is anticipated to rise to 23.6 million by 20301. Although some developed countries have observed a decline in mortality from cardiovascular diseases in recent times, developing countries are still facing an escalating burden2. In South Asia, ischemic heart disease is the leading cause of mortality. It accounts for 10.6% of total reported fatalities, equating to 1.8 million deaths, and contributes to more than half of cardiovascular mortality3. Despite this scenario, very little is known about the exact prevalence of coronary artery disease in Bangladesh. Recent data suggests that coronary artery disease prevalence ranges from 1.85% to 3.4% in rural areas and 19.6% in urban settings4. According to the Global Burden of Disease Study, as of 2020, the South Asian region, which includes India, Pakistan, Bangladesh, and Nepal, was projected to bear a disproportionate burden of atherothrombotic cardiovascular disease than any other region5.

Procalcitonin (PCT) is a 116-amino acid polypeptide precursor of calcitonin and is elevated in conditions associated with bacterial infections, such as sepsis6 and post-cardiac surgery7. Given the inflammatory response accompanying acute myocardial infarction (AMI), multiple studies have explored the potential association between PCT levels and AMI severity and prognosis. While some studies found no clear association8, others demonstrated correlations between PCT release and established prognostic markers9 as well as its elevation being associated with severe heart failure, resuscitated cardiac arrest, or concurrent bacterial infection10.

Subsequent research delved into the role of PCT in acute coronary syndrome (ACS) finding its notable associations with major adverse cardiac and cerebrovascular events (MACCE). Observational studies indicate significantly higher PCT levels in ACS patients being identified as a ‘higher risk’ group of ACS patients for short and long-term mortality and experiencing cardiogenic shock post-ST-elevation acute myocardial infarction (STEMI)11. Moreover, prospective cohort studies highlight a nearly 50% higher relative risk of MACCE at 12 months post-myocardial infarction (MI) in individuals with elevated PCT levels, with a predominant association with patient mortality during follow-up12. Larger prospective studies further confirm elevated plasma PCT levels in patients experiencing MACCE, underscoring its potential prognostic value in ACS13.

There is a paucity of data regarding acute phase major adverse cardiac and cerebrovascular events (MACCE) following ST-segment elevation myocardial infarction (STEMI) in Bangladesh. A recent study at the National Institute of Cardiovascular Disease (NICVD), revealed that 6.2% of patients encountered an in-hospital adverse event, and 7.5% experienced events within the 30 days following discharge14. Another cross-sectional observational study also had similar findings where about 7.8% of the patients had MACCE events15.

However, the role of peripheral PCT concentration in predicting ST-segment elevation myocardial infarction (STEMI) prognosis in Bangladeshi individuals remains unexplored. Our study aims to examine the relationship between PCT levels at admission and clinical outcomes post-STEMI to get a more comprehensive understanding of PCT's prognostic significance. This study focuses on MACCE as the primary endpoint during a one-month follow-up, utilizing chemiluminescence immunoassay (CLIA) technology to measure PCT levels.

**Materials and methods:**

**Study Design and Setting**:

Our study was a prospective observational study that was conducted at the Department of Cardiology at BSMMU from October 2020 to September 2021 after receiving approval from the Institutional Review Board (IRB).

**Sample size and population:**

The sample size was predetermined to be 54 using an appropriate formula for comparative study. Enrollment involved STEMI patients who were admitted within the first 12 hours of symptom onset. STEMI was defined clinically as chest pain lasting >20 minutes, ECG evidence of ST elevation >1mm in >2 contiguous leads, or presumably new LBBB or true Posterior MI with ST depression of >1mm in >2 contiguous anterior leads V1-V3 with a positive terminal T wave. Posterior MI was further confirmed by concomitant ST-segment elevation ≥ 0.5 mm recorded in leads V7–V9.

**Data collection:**

The purpose of the study was thoroughly explained to each participant and informed written consent was obtained. Detailed demographic information, risk factors, and clinical history were recorded. Various diagnostic measures, including 12-lead ECG, Troponin I, CK-MB, serum creatinine, serum procalcitonin, HbA1c, and echocardiography, were conducted during the enrollment. Blood samples, collected aseptically, underwent biochemical investigations, including the measurement of procalcitonin using LIAISON BRAHMS PCT II GEN assay with chemiluminescence immunoassay (CLIA) technology. The study employed rigorous procedures to ensure data integrity and quality throughout the process.

### **Statistical analysis:**

### Statistical analyses of the study were planned and reviewed by the investigators and guide. Following data editing, statistical analysis was conducted using the Statistical Package for Social Science (SPSS) version 25.0 for Windows. Numerical data were presented as mean with standard deviation (SD) and assessed using the Student's t-test. Categorical data were expressed as frequencies and percentages, and the Chi-Square test was employed for analysis. To identify independent predictors of Major Adverse Cerebrovascular Events (MACE), both univariate and multivariate logistic regression analyses were employed. A significance level of p < 0.05 was considered statistically significant.

## **Results:**

Table 1: Distribution of MACCE according to admission PCT

| MACCE Status | Group 1 (n=27) | Group 2 (n=27) | P value |
| --- | --- | --- | --- |
| Low PCT | High PCT |
| MACCE n(%) | 24 (54.5) | 20 (45.5) | 0.038 |
| Non MACCE n(%) | 3 (30) | 7 (70) |

In Table 1, MACCE was evident in 3 patients in the low PCT group and 7 patients in the high PCT group, with a significant P-value of 0.038 from the chi-square test.

Table 2: Association of plasma procalcitonin with the onset of MACCE through univariate &

multivariate logistic regression analysis

|  | Univariate | Multivariateb |
| --- | --- | --- |
|  | Odds Ratio | 95% CIa | P value | Adjusted Odds Ratio | 95% CI | P value |
| Age  | 1.171 | 0.874-2.745 | 0.762 | 1.065 | 0.649-1.928 | 0.819 |
| Gender | 0.723 | 0.308 - 1.837 | 0.981 | 0.638 | 0.482 - 1.742 | 0.762  |
| BMIa | 1.420  | 1.021-3.264  | 0.034 | 1.099 | 0.819-2.532 | 0.468 |
| Smoker | 2.180 | 0.949-3.146 | 0.485 | 1.843 | 0.842-2.946 | 0.655 |
| HTN | 1.923 | 0.824-2.860 | 0.357 | 1.645 | 0.698-2.510 | 0.467 |
| DM | 2.415 | 1.249-3.228 | 0.001 | 2.089 | 1.054-2.678 | 0.001 |
| Dyslipidemia | 3.142 | 1.098-5.024 | 0.001 | 2.564 | 0.956-4.662 | 0.068 |
| Family History | 1.185 | 0.894-2.210 | 0.339 | 0.841 | 0.688-1.658 | 0.384 |
| Troponin I | 0.292 | 0.081-1.829 | 0.519 | 0.189 | 0.041-1.015 | 0.954 |
| Procalcitonin | 4.541 | 2.119-6.521 | 0.001 | 3.475 | 1.962-5.546 | 0.001 |
| LVEFa | 3.689 | 1.056-4.969 | 0.026 | 2.958 | 1.01- 3.412 | 0.034 |
| CRPa | 1.902 | 0.873-3.021 | 0.398 | 1.428 | 0.592- 2.429 | 0.867 |

aCI: confidence interval; BMI: body mass index; DM: diabetes mellitus; LVEF: Left ventricular ejection fraction; CRP: C reactive protein

bMultivariable adjusted odds ratio were adjusted with rest of the other variables

Table 2 shows that higher admission PCT levels pose a higher risk of MACCE (OR: 4.541, 95% CI: 2.119 – 6.521; AOR: 3.475, 95% CI: 1.962 - 5.546), indicating a 3.5 times increased risk per unit PCT increase. Confounders include age, sex, BMI, hypertension, dyslipidemia, smoking, family history, troponin-I, CRP, and reduced ejection fraction (LVEF<40%).

Table 3: Adjusted odds ratio for MACCE considering Procalcitonin, Treatment

Modalities, and STEMI Surface involvement

|  | 95% CI |
| --- | --- |
|  | AOR | Lower | Upper | P value |
| Low PCT | 1 |  |  |  |
| High PCT | 2.608 | 1.337 | 7.674 | 0.001 |
| Modalities |  |  |  | 0.991 |
| Thrombolysis | 1 |  |  |  |
| Pharmacoinvasive | 0.974 | 0.155 | 6.111 | 0.977 |
| Routine PCI | 0.736 | 0.118 | 4.615 | 0.744 |
| Medical Management | 0.024 | 0.001 | 1.054 | 0.999 |
| Surface |  |  |  | 0.949 |
| Anterior | 1 |  |  |  |
| Inferior | 0.622 | 0.130 | 2.967 | 0.551 |
| Lateral | 0.384 | 0.114 | 1.214 | 0.954 |
| Posterior | 0.062 | 0.021 | 1.022 | 0.994 |

aAOR: adjusted odds ratio

bCI: confidence interval

In Table 3, higher admission PCT levels are seen associated with a higher risk of MACE (AOR: 2.608, 95% CI: 1.337-7.674), suggesting a 2.608 times increased risk per unit PCT increase. Confounders include treatment modalities and STEMI surface involvement.

## **Conclusion:**

In conclusion, our study highlights a significant association between elevated serum procalcitonin (PCT) levels as an increased risk of major adverse cardiac and cerebrovascular events (MACCE). This underscores the potential independent predictive value of peripheral PCT concentration for adverse outcomes in STEMI, emphasizing its relevance as a prognostic biomarker. These findings contribute to the understanding of risk stratification in STEMI patients and suggest the utility of serum PCT in predicting poor prognosis.